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*DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES;
OP=AND*

L1	(zn or zinc).clm. same (proteinase or protease or peptidase or proteolytically or proteolytic).clm.	44	L1
L2	L1 and (nucleic or polynucleotide or nucleotide or gene or genetic or genetically or encodes or dna or cdna or rna or mrna or poly-nucleotide or nucleic).clm.	18	L2

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L2: Entry 12 of 18

File: USPT

Oct 8, 2002

DOCUMENT-IDENTIFIER: US 6461850 B2

TITLE: Isolated nucleic acid molecules encoding protease proteins, and uses thereof

CLAIMS:

1. An isolated nucleic acid molecule encoding a zinc protease, wherein the nucleic acid molecule consists of a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO:2; (b) a nucleotide sequence consisting of SEQ ID NO:1; and (c) a nucleotide sequence consisting of SEQ ID NO:3.
2. A nucleic acid vector comprising the nucleic acid molecule of claim 1.
5. An isolated polynucleotide encoding a zinc protease wherein the polynucleotide consists of the nucleotide sequence set forth in SEQ ID NO: 1.
6. An isolated polynucleotide encoding a zinc protease wherein the polynucleotide consists of the nucleotide sequence set forth in SEQ ID NO: 3.
8. A vector according to claim 2, wherein said isolated nucleic acid molecule is inserted into said vector in proper orientation and correct reading frame such that the protein of SEQ ID NO:2 may be expressed by a cell transformed with said vector.
9. A vector according to claim 8, wherein said isolated nucleic acid molecule is operatively linked to a promoter sequence.
10. An isolated nucleic acid molecule consisting of a nucleotide sequence that is completely complementary to the nucleotide sequences of claim 1.

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[\[Keywords\]](#) [\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

General information about the entry

Entry name	HCE1_ORYLA
Primary accession number	P31580
Secondary accession numbers	None
Entered in Swiss-Prot in	Release 26, July 1993
Sequence was last modified in	Release 26, July 1993
Annotations were last modified in	Release 41, June 2002
Name and origin of the protein	
Protein name	High choriolytic enzyme 1 [Precursor]
Synonyms	EC <u>3.4.24.67</u> Hatching enzyme zinc-protease HCE 1 subunit Choriolysin H 1
Gene name	HCE 23
From	<u>Oryzias latipes</u> (Medaka [TaxID: fish) (Japanese ricefish) <u>8090</u>)
Taxonomy	<u>Eukaryota</u> ; <u>Metazoa</u> ; <u>Chordata</u> ; <u>Craniata</u> ; <u>Vertebrata</u> ; <u>Euteleostomi</u> ; <u>Actinopterygii</u> ; <u>Neopterygii</u> ; <u>Teleostei</u> ; <u>Euteleostei</u> ; <u>Neoteleostei</u> ; <u>Acanthomorpha</u> ; <u>Acanthopterygii</u> ; <u>Percomorpha</u> ; <u>Atherinomorpha</u> ; <u>Beloniformes</u> ; <u>Adrianichthyidae</u> ; <u>Oryziinae</u> ; <u>Oryzias</u> .
References	

[1] SEQUENCE FROM NUCLEIC ACID, AND SEQUENCE OF 71-119 AND 208-223.

TISSUE=Embryo;

MEDLINE=93012471; PubMed=1397682; [NCBI, ExPASy, EBI, Israel, Japan]

Yasumasu S., Yamada K., Akasaka K., Mitsunaga K., Iuchi I., Shimada H., Yamagami K.;

"Isolation of cDNAs for LCE and HCE, two constituent proteases of the hatching enzyme of *Oryzias latipes*, and concurrent expression of their mRNAs during development.";

Dev. Biol. 153:250-258(1992).

Comments

- **FUNCTION:** PARTICIPATES IN THE BREAKDOWN OF THE EGG ENVELOPE, WHICH IS DERIVED FROM THE EGG EXTRACELLULAR MATRIX, AT THE TIME OF HATCHING. THUS ALLOWING THE NEWLY HATCHED FISH TO SWIM FREE. HCE BINDS TIGHTLY TO THE EGG ENVELOPE WHILE IT EXERTS THE CHORIOLYTIC SWELLING ACTION.
- **CATALYTIC ACTIVITY:** Hydrolysis of the inner layer of fish egg envelope. Also hydrolyzes casein and small molecule substrates such as Suc-Leu-Leu-Val-Tyr-|-MCA.
- **COFACTOR:** Binds 1 zinc ion per subunit (*By similarity*).
- **SUBCELLULAR LOCATION:** STORED AS PROENZYMES IN THE ZYMOGEN GRANULES.
- **DEVELOPMENTAL STAGE:** PRODUCTION OF THE PROTEIN STARTS IN DAY 2 TO DAY 3 EMBRYOS AND INCREASES THEREAFTER UNTIL HATCHING.
- **PTM:** O-GLYCOSYLATED (*PROBABLE*).
- **MISCELLANEOUS:** IN MEDAKA THE HATCHING ENZYME SYSTEM IS COMPOSED OF TWO DISTINCT PROTEASES, THE HIGH CHORIOLYTIC ENZYME (HCE), OF WHICH THERE ARE TWO ISOFORMS, AND THE LOW CHORIOLYTIC ENZYME (LCE).
- **SIMILARITY:** BELONGS TO PEPTIDASE FAMILY M12A.

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Cross-references

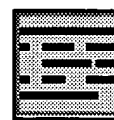
EMBL	M96170; AAA49438.1; [EMBL / GenBank / DDBJ] - [CoDingSequence]
PIR	B48826; B48826.
HSSP	P07584; 1IAE. [HSSP ENTRY / PDB]
MEROPS	M12.007; -.
InterPro	IPR001506; Astacin. IPR000130; Zn_MTpeptdse. <u>Graphical view of domain structure.</u>
Pfam	PF01400; Astacin; 1.
SMART	SM00235; ZnMc; 1.
PROSITE	PS00142; ZINC_PROTEASE; 1.
ProDom	[Domain structure / <u>List of seq. sharing at least 1 domain</u>].
BLOCKS	<u>P31580.</u>
ProtoNet	<u>P31580.</u>
ProtoMap	<u>P31580.</u>
PRESAGE	<u>P31580.</u>
DIP	<u>P31580.</u>
ModBase	<u>P31580.</u>
SWISS-2DPAGE	<u>Get region on 2D PAGE.</u>

Keywords

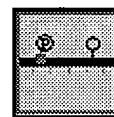
Hydrolase; Metalloprotease; Zinc; Glycoprotein; Zymogen; Signal.

Features

Key	From	To	Length	Description
SIGNAL	<u>1</u>	<u>20</u>	20	
PROPEP	<u>21</u>	<u>70</u>	50	ACTIVATION PEPTIDE.
CHAIN	<u>71</u>	<u>270</u>	200	HIGH CHORIOLYTIC ENZYME 1.
METAL	<u>169</u>	<u>169</u>		ZINC (CATALYTIC) (BY SIMILARITY).
ACT_SITE	<u>170</u>	<u>170</u>		BY SIMILARITY.
METAL	<u>173</u>	<u>173</u>		ZINC (CATALYTIC) (BY SIMILARITY).
METAL	<u>179</u>	<u>179</u>		ZINC (CATALYTIC) (BY SIMILARITY).
CARBOHYD	<u>53</u>	<u>53</u>		N-LINKED (GLCNAC...) (POTENTIAL).



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Sequence information

Length: 270 AA [This is the length of the unprocessed precursor]	Molecular weight: 30392 Da [This is the MW of the unprocessed precursor]	CRC64: D85C972906E3735A [This is a checksum on the sequence]
--	--	--

10	20	30	40	50	60
MNLAPSTCLL	LLFLLDIAQA	LPVWDEEGHE	EGHEEGDGDD	FVDITTRILT	SNNNTDQLLL
70	80	90	100	110	120
EGDLVAPTNR	NAMKCWSSSC	FWKKASNGLV	VIPYVISSEY	SGGEVATIEG	AMRAFNGKTC
130	140	150	160	170	180
IRFVVRTNEY	DFISVSKTG	CYSELGRKGG	QQELSINRGG	CMYSGIIQHE	LNHALGFQHE
190	200	210	220	230	240
QTRSDRDSYV	RINWENIIPA	SAYNFNKHDT	NNLNTPYDYS	SIMHYGRDAF	SIAYGRDSIT
250	260	270			
PIPNNPVP	QIRNGMSRWDI	TRINVLNCR			

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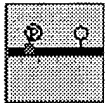
Sequence analysis tools:

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[Dotlet](#) (Java)



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General information about the entry

Entry name	Q54249
Primary accession number	Q54249
Secondary accession numbers	None
Entered in TrEMBL in	Release 01, November 1996
Sequence was last modified in	Release 01, November 1996
Annotations were last modified in	Release 19, December 2001

Name and origin of the protein

Protein name	Coaggregation mediating adhesin (scaA), ATP binding protein, hydrophobic membrane protein, and zinc metalloprotease
Synonyms	None
Gene name	None
From	<u>Streptococcus gordonii</u> [TaxID: 1302]
Taxonomy	<u>Bacteria</u> ; <u>Firmicutes</u> ; <u>Lactobacillales</u> ; <u>Streptococcaceae</u> ; <u>Streptococcus</u> .

References

- [1] SEQUENCE FROM NUCLEIC ACID.
 STRAIN=PK488;
 MEDLINE=95012638; PubMed=7927711; [[NCBI](#), [ExPASy](#), [EBI](#), [Israel](#), [Japan](#)]
[Kolenbrander P.E.](#), [Andersen R.N.](#), [Ganeshkumar N.](#);
 "Nucleotide sequence of the *Streptococcus gordonii* PK488 coaggregation adhesin gene, *scaA*, and ATP-binding cassette.";
[Infect. Immun.](#) 62:4469-4480(1994).

Comments

None

Cross-references

EMBL	L11577; AAA71949.1; [EMBL / GenBank / DDBJ] [CoDingSequence]
ProDom	[Domain structure / List of seq. sharing at least 1 domain].
ProtoMap	Q54249 .
PRESAGE	Q54249 .
ModBase	Q54249 .
SWISS-2DPAGE	Get region on 2D PAGE .

Keywords

None

Features

None

Sequence information

Length: 229 AA	Molecular weight: 25107 Da	CRC64: 37B98C9EC1E2F780 [This is a checksum on the sequence]
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10	20	30	40	50	60
MLLHGVTTVE	AKSGYGLDWE	TEKRQLDVVG	ALDRDHDIDL	VSTFMAAHAV	PPEYKGRSQE
70	80	90	100	110	120
YLELIVEEML	PRVKAENLAE	FCDIFCEKGV	FTADESRYLL	SKAKEMGFKL	RIHADEMESI
130	140	150	160	170	180
GGVDVAAELG	ATSAEHLMAA	TDEGIRKMAE	AKVIGNLLPA	TTFSLMEDTY	APARKMLEAG
190	200	210	220		
MAITLTTDSN	PGSCPTANLQ	FVMQLGCFMM	RSDASGSPQR	CNHQCGLLS	

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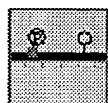


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[\[Keywords\]](#)
[\[Features\]](#)
[\[Sequence\]](#)
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General information about the entry

Entry name	O25144
Primary accession number	O25144
Secondary accession numbers	None
Entered in TrEMBL in	Release 05, January 1998
Sequence was last modified in	Release 05, January 1998
Annotations were last modified in	Release 19, December 2001

Name and origin of the protein

Protein name	Zinc-metallo protease
Synonym	YJR117W
Gene name	<u>HP0382</u>
From	<u>Helicobacter pylori</u> [TaxID: (<u>Campylobacter pylori</u>) 210]
Taxonomy	<u>Bacteria</u> ; <u>Proteobacteria</u> ; <u>epsilon</u> <u>subdivision</u> ; <u>Helicobacter group</u> ; <u>Helicobacter</u> .

References

[1] SEQUENCE FROM NUCLEIC ACID.

STRAIN=26695 / ATCC 700392;

MEDLINE=97394467; PubMed=9252185; [[NCBI](#), [ExPASy](#), [EBI](#), [Israel](#), [Japan](#)]

[Tomb J.-F.](#), [White O.](#), [Kerlavage A.R.](#), [Clayton R.A.](#), [Sutton G.G.](#), [Fleischmann R.D.](#), [Ketchum K.A.](#), [Klenk H.-P.](#), [Gill S.](#), [Dougherty B.A.](#), [Nelson K.](#), [Quackenbush J.](#), [Zhou L.](#), [Kirkness E.F.](#), [Peterson S.](#), [Loftus B.](#), [Richardson D.](#), [Dodson R.](#), [Khalak H.G.](#), [Glodek A.](#), [McKenney K.](#), [FitzGerald L.M.](#), [Lee N.](#), [Adams M.D.](#), [Hickey E.K.](#), [Berg D.E.](#), [Gocayne J.D.](#), [Utterback T.R.](#), [Peterson J.D.](#), [Kelley J.M.](#), [Cotton M.D.](#), [Weidman J.M.](#), [Fujii C.](#), [Bowman C.](#), [Watthey L.](#), [Wallin E.](#), [Hayes W.S.](#), [Borodovsky M.](#), [Karp P.D.](#), [Smith H.O.](#), [Fraser C.M.](#), [Venter J.C.](#);

"The complete genome sequence of the gastric pathogen *Helicobacter pylori*.";

Nature 388:539-547(1997).

Comments

None

Cross-references

EMBL	AE000555; AAD07451.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
MEROPS	M48.008 ; -.	
TIGR	HP0382 ; -.	
InterPro	IPR001915 ; Peptidase_M48. Graphical view of domain structure.	
Pfam	PF01435 ; Peptidase_M48; 1.	
ProDom	[Domain structure / List of seq. sharing at least 1 domain].	
ProtoMap	O25144 .	
PRESAGE	O25144 .	
ModBase	O25144 .	
SWISS-2DPAGE	Get region on 2D PAGE.	

Keywords

Hypothetical protein; Protease; Complete proteome.

Features

None

Sequence information

Length: 407 AA

Molecular weight: 46276 Da

CRC64: 1A44765F3092BD07 [This is a checksum on the sequence]

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QLSIISQILD	GIIFAGWVFF	GLTHLEDLTH	YLNLPETLGY	LVFALLFLAI	QSVLALPISY
130	140	150	160	170	180
YTTMHLDKF	GFSKVSLSLF	FKDFFKGLSL	TLSVGLLLIY	TLIMIIEHVE	HWEISSFFV
190	200	210	220	230	240
FVFMILANLF	YPKIAQLFNQ	FTPLNNRDLE	SQIEGMMDKV	GFKSEGIFVM	DASKRDGRLN
250	260	270	280	290	300
AYFGGLGKNK	RVVLFDTLIS	KVGTEGLLAI	LGHELGHFKN	KDLLKSLGIM	GGLLALVFAL
310	320	330	340	350	360
IAHLPLPVFE	GFNVSQTPAS	LIAILLFLP	VFSFYAMPLI	GFFSRKNEYN	ADKFGASLSS
370	380	390	400		
KEVLAKALVS	IVSENKAFPY	SHPFYVFLHF	THPPLLERLK	ALDYEIE	

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Tools

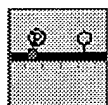
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File 155:MEDLINE(R) 1966-2003/Feb W2
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Set	Items	Description
---	-----	-----
?e	zinc	protease

Ref	Items	RT	Index-term
E1	6		ZINC PHTHALOCYANINE SULFONATE
E2	34		ZINC POLYACRYLATE
E3	0		*ZINC PROTEASE
E4	465		ZINC PROTOPORPHYRIN
E5	62		ZINC PYRITHIONE
E6	351	5	ZINC RADIOISOTOPES
E7	10		ZINC RADIOISOTOPES --ADMINISTRATION AND DOSAGE
E8	6		ZINC RADIOISOTOPES --ADVERSE EFFECTS --AE
E9	19		ZINC RADIOISOTOPES --ANALYSIS --AN
E10	2		ZINC RADIOISOTOPES --BLOOD --BL
E11	1		ZINC RADIOISOTOPES --CHEMISTRY --CH
E12	137		ZINC RADIOISOTOPES --DIAGNOSTIC USE --DU

Enter P or PAGE for more

?s (zn or zinc?) (2n) (protease? or proteinase? or peptidase?)

	13370	ZN
	51192	ZINC?
	65433	PROTEASE?
	27443	PROTEINASE?
	7314	PEPTIDASE?
S1	334	(ZN OR ZINC?) (2N) (PROTEASE? OR PROTEINASE? OR PEPTIDASE?)

?s s1 and (pylori or pylroi or pyloris or pyloridis or helicobacter? or hpylori?)

	334	S1
	16984	PYLORI
	0	PYLROI
	10	PYLORIS
	176	PYLORIDIS
	16623	HELICOBACTER?
	2	HPYLORI?
S2	0	S1 AND (PYLORI OR PYLROI OR PYLORIS OR PYLORIDIS OR HELICOBACTER? OR HPYLORI?)

?s s1/1997:2003

	334	S1
	2893533	PY=1997 : PY=2003
S3	132	S1/1997:2003

?s s1 not s3

	334	S1
	132	S3
S4	202	S1 NOT S3

?s s4 and (dna? or cdna? or nucleic? or polynucleot? or nucleotid? or gene?)

	202	S4
	680602	DNA?
	92709	CDNA?
	155296	NUCLEIC?
	8889	POLYNUCLEOT?
	171300	NUCLEOTID?
	1969781	GENE?
S5	64	S4 AND (DNA? OR CDNA? OR NUCLEIC? OR POLYNUCLEOT? OR NUCLEOTID? OR GENE?)

?s s1/ti

S6	47	S1/TI
----	----	-------

?s s6 not s3

	47	S6
	132	S3
S7	36	S6 NOT S3

?s s7 and s5

	36	S7
--	----	----

64 S5

S8

12 S7 AND S5

?t s8/9/all

8/9/1

• DIALOG(R) File 155:MEDLINE(R)

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09200566 97101029 PMID: 8945556

Surface Zn - proteinase as a molecule for defense of Leishmania mexicana amazonensis promastigotes against cytolysis inside macrophage phagolysosomes.

Seay M B; Heard P L; Chaudhuri G

Division of Biomedical Sciences, Meharry Medical College, Nashville, Tennessee 37208, USA.

Infection and immunity (UNITED STATES) Dec 1996, 64 (12) p5129-37,

ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: 3 S06 GM008037-21S1; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The role of the surface membrane **Zn - proteinase** in protecting the cellular integrity of the macrophage parasite *Leishmania mexicana amazonensis* from intraphagolysosomal cytolysis was studied. These cells lose their infectivity to host macrophages after prolonged cultivation in axenic growth medium. The virulent and attenuated variants of the parasite cells were cloned. Failure of these attenuated parasite cells to survive inside macrophage phagolysosomes is associated with 20- to 50-fold reduction in the expression of surface gp63 protein. In situ inhibition of gp63 proteinase activity inside *Leishmania*-infected macrophage phagolysosomes with targeted delivery of an inhibitor of gp63 proteinase activity, 1,10-phenanthroline, selectively eliminated intracellular *Leishmania* amastigotes, further suggesting the importance of this proteinase in phagolysosomal survival of the parasite. An upstream sequence (US) of the gp63 **gene** was cloned in front of the bacterial chloramphenicol acetyltransferase (CAT) **gene** in plasmid pCATbasic. Transfection of *L. mexicana amazonensis* cells with this recombinant plasmid showed that expression of the CAT **gene** from this US is 15- to 20-fold higher in virulent clones than in avirulent clones of the parasite. Band shift analysis with the cloned US also showed that binding of protein(s) was 15- to 20-fold higher in virulent cell extract than in avirulent cell extract. Coating of attenuated cells or liposomes with proteolytically active gp63 protects them from degradation inside macrophage phagolysosomes. These results suggest a novel mechanism of survival of this phagolysosomal parasite with the help of its surface **Zn - proteinase**.

Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *Endopeptidases--analysis--AN; **Leishmania mexicana* --enzymology--EN; *Macrophages--parasitology--PS; *Phagosomes--parasitology--PS; *Leishmania mexicana*--parasitology--PS

Enzyme No.: EC 3.4.- (Endopeptidases)

Record Date Created: 19970108

8/9/2

DIALOG(R) File 155:MEDLINE(R)

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09124949 97014153 PMID: 8860988

The metzincin-superfamily of zinc - peptidases .

Bode W; Grams F; Reinemer P; Gomis-Ruth F X; Baumann U; McKay D B; Stocker W

Max-Planck-Institut fur Biochemie, Am Klopferspitz, Martinsried, Germany.

Advances in experimental medicine and biology (UNITED STATES) 1996,

389 p1-11, ISSN 0065-2598 Journal Code: 0121103

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
(49 Refs.)
Tags: Support, Non-U.S. Gov't
Descriptors: Metalloendopeptidases-- **genetics** --GE; *Multigene Family;
Amino Acid Sequence; Binding Sites; Catalysis; Metalloendopeptidases
--chemistry--CH; Models, Molecular; Molecular Sequence Data; Sequence
Homology, Amino Acid; Structure-Activity Relationship
Enzyme No.: EC 3.4.24 (Metalloendopeptidases)
Record Date Created: 19970306

8/9/3

DIALOG(R) File 155:MEDLINE(R)

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08886284 96228688 PMID: 8688560

Biochemical and functional analysis of the YME1 gene product, an ATP and zinc -dependent mitochondrial protease from S. cerevisiae.

Weber E R; Hanekamp T; Thorsness P E

Department of Molecular Biology, University of Wyoming, Laramie
82071-3944, USA.

Molecular biology of the cell (UNITED STATES) Feb 1996, 7 (2)
p307-17, ISSN 1059-1524 Journal Code: 9201390

Contract/Grant No.: GM47390; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Inactivation of YME1 in yeast causes several distinct phenotypes: an increased rate of **DNA** escape from mitochondria, temperature-sensitive growth on nonfermentable carbon sources, extremely slow growth when mitochondrial **DNA** is completely absent from the cell, and altered morphology of the mitochondrial compartment. The protein encoded by YME1, Ymelp, contains two highly conserved sequence elements, one implicated in the binding and hydrolysis of ATP, and the second characteristic of active site residues found in neutral, **zinc** -dependent **proteases**. Both the putative ATPase and **zinc** -dependent **protease** elements are necessary for the function of Ymelp as **genes** having mutations in critical residues of either of these motifs are unable to suppress any of the phenotypes exhibited by yme1 deletion strains. Ymelp co-fractionates with proteins associated with the mitochondrial inner membrane, is tightly associated with this membrane, and is oriented with the bulk of the protein facing the matrix. Unassembled subunit II of cytochrome oxidase is stabilized in yme1 yeast strains. The data support a model in which Ymelp is an ATP and **zinc** -dependent **protease** associated with the matrix side of the inner mitochondrial membrane. Subunit II of cytochrome oxidase, when not assembled into a higher order complex, is a likely substrate of Ymelp.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Adenosine Triphosphate--metabolism--ME; *Adenosinetriphosphatase--metabolism--ME; *Mitochondria--enzymology--EN; *Saccharomyces cerevisiae--enzymology--EN; *Zinc--metabolism--ME; Adenosinetriphosphatase --chemistry--CH; Adenosinetriphosphatase-- **genetics** --GE; Base Sequence; Cytochrome-c Oxidase--metabolism--ME; **DNA**, Fungal; Heat-Shock Proteins --chemistry--CH; Heat-Shock Proteins-- **genetics** --GE; Heat-Shock Proteins --metabolism--ME; Molecular Sequence Data; Mutagenesis, Site-Directed; Serine Endopeptidases--chemistry--CH; Serine Endopeptidases-- **genetics** --GE; Serine Endopeptidases--metabolism--ME

CAS Registry No.: 0 (DNA, Fungal); 0 (Heat-Shock Proteins); 56-65-5 (Adenosine Triphosphate); 7440-66-6 (Zinc)

Enzyme No.: EC 1.9.3.1 (Cytochrome-c Oxidase); EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.53 (endopeptidase La); EC 3.6.1.- (YME1 protein); EC 3.6.1.3 (Adenosinetriphosphatase)

8/9/4

DIALOG(R) File 155:MEDLINE(R)

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08588167 95345460 PMID: 7620164

Distribution of carboxypeptidase M on lymphoid and myeloid cells parallels the other zinc-dependent proteases CD10 and CD13.

de Saint-Vis B; Cupillard L; Pandrau-Garcia D; Ho S; Renard N; Grouard G; Duvert V; Thomas X; Galizzi J P; Banchereau J; et al

Laboratory for Immunological Research, Schering-Plough, Dardilly, France.

Blood (UNITED STATES) Aug 1 1995, 86 (3) p1098-105, ISSN 0006-4971

Journal Code: 7603509

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Monoclonal antibody (MoAb) M27 was **generated** after immunization of mice with the human B-lineage acute lymphoblastic leukemia cell line Pre-ALP. Under reducing conditions, MoAb M27 precipitated a 60-kD surface-membrane molecule from Pre-ALP cells. Expression cloning of Pre-ALP **cdna** showed that M27 recognizes carboxypeptidase M (CPM), a cell-surface, **zinc**-dependent **protease** known to cleave off basic C-terminal amino acids from peptide hormones. Using M27 antibody, CPM was detected only at discrete B lymphocyte developmental stages, namely on committed precursors and on germinal center cells. CPM was also expressed on mature T cells, mainly after activation. These results provide the first description of a carboxy-peptidase on lymphoid cells. In addition, CPM was found on granulocytes and monocytes, but not on their progenitors. Strikingly, CPM was present only on CD38+ cells, irrespective of lineage affiliation. Of interest, CPM displayed a largely overlapping distribution with the CD10 and CD13 peptidases, with which it shares common substrates (enkephalins, bradykinin). Collectively, the present data show a previously unrecognized distribution pattern of CPM on lymphoid and myeloid cells and suggest that CPM may cooperate with CD10 and CD13 to regulate biologic activity of peptide hormones on leukocytes.

Tags: Animal; Case Report; Human

Descriptors: *Antigens, CD13--metabolism--ME; *Bone Marrow--enzymology--EN; *Lymphocytes--enzymology--EN; *Metalloendopeptidases--metabolism--ME; *Neprilysin--metabolism--ME; Adult; Antibodies, Monoclonal--immunology--IM; Antigens, Differentiation--analysis--AN; B-Lymphocytes--cytology--CY; B-Lymphocytes--enzymology--EN; Bone Marrow--embryology--EM; Bone Marrow Cells; Cell Differentiation; Child; Immunophenotyping; Lymphocyte Transformation; Mice; Mice, Inbred BALB C; Nucleosidases--analysis--AN; T-Lymphocytes--enzymology--EN; Zinc--physiology--PH

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antigens, Differentiation); 7440-66-6 (Zinc)

Enzyme No.: EC 3.2.2. (Nucleosidases); EC 3.2.2.- (T10 antigen); EC 3.4.11.2 (Antigens, CD13); EC 3.4.17.12 (carboxypeptidase M); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.11 (Neprilysin)

Record Date Created: 19950829

8/9/5

DIALOG(R) File 155:MEDLINE(R)

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07959179 94094847 PMID: 8269943

General occurrence of binding synergism in zinc proteases and its possible significance.

Chan W W; Pfuetzner R A

Department of Biochemistry, McMaster University, Hamilton, Canada.

European journal of biochemistry / FEBS (GERMANY) Dec 1 1993, 218 (2) p529-34, ISSN 0014-2956 Journal Code: 0107600

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The observation of binding synergism has been successfully extended to include carboxypeptidases A and B. The behaviour of these two enzymes follows the same pattern previously found for three other **Zn - proteases**. Thus in all cases examined, the affinity of a suitable Zn-ligand is increased in the presence of a compound (specificity probe) which contains the key structural features of specific substrates. A bifunctional ligand such as phosphonoacetate is particularly useful for **generating** synergism in both carboxypeptidases. Presumably the carboxylate moiety binds to the C-terminal recognition site while the other functional group interacts with the metal ion. Several basic compounds (e.g. methyl guanidine) act as effective specificity probes for carboxypeptidase B while phenol and other hydrophobic substances serve this purpose in carboxypeptidase A. The above phenomenon appears to be a mechanism designed to enhance catalytic efficiency through a substrate-induced conformational change. We postulate that there is a requirement for at least one ionizable group at the active site. The proposed mechanism keeps this group in the correct ionization state in the presence of water and increases its reactivity after exclusion of water by substrate binding. We suggest the term xerophilic shift for this process. Since proton transfer is a common process in enzyme reactions, the xerophilic-shift mechanism may play a similar role in many instances. It should therefore be possible to detect binding synergism in a wide variety of enzymes.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Carboxypeptidases--metabolism--ME; *Zinc--metabolism--ME; Binding Sites; Cattle; Cross-Linking Reagents; Ligands; Pancreas--enzymology--EN; Swine

CAS Registry No.: 0 (Cross-Linking Reagents); 0 (Ligands); 7440-66-6 (Zinc)

Enzyme No.: EC 3.4.-. (Carboxypeptidases); EC 3.4.17.1 (carboxypeptidase A); EC 3.4.17.2 (carboxypeptidase B)

Record Date Created: 19940203

8/9/6

DIALOG(R) File 155:MEDLINE(R)

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07705399 93232072 PMID: 8473348

Purification and characterization of a novel zinc - proteinase from cultures of *Aeromonas hydrophila*.

Loewy A G; Santer U V; Wieczorek M; Blodgett J K; Jones S W; Cheronis J C
Department of Biology, Haverford College, Pennsylvania 19041.

Journal of biological chemistry (UNITED STATES) Apr 25 1993, 268 (12)
p9071-8, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: AM 34503; AM; NIADDK

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

While searching for an enzyme capable of breaking epsilon-(gamma-Glu)-Lys isopeptide bonds cross-linking protein chains, we purified a metallo-proteinase which mimics the action of an isopeptidase on the gamma-chain dimers of cross-linked fibrin. The enzyme is present in the growth medium of the bacterium *Aeromonas hydrophila*, isolated from the intestinal tract of the leech *Hirudo medicinalis*. It is a 19-kDa protein which specifically hydrolyzes the Gly-Ala peptide bond within the Gly-Gly-Ala sequence, located near the cross-link site in the gamma-chain dimer of fibrin. Substrate specificity studies with a number of synthetic peptides suggest that the enzyme prefers Gly-Gly or acetyl-Gly in the P2 and P1 positions, respectively (Schechter, I., and Berger, A. (1967) Biochem. Biophys. Res. Commun. 27, 157-162). Nonpolar amino acid residues

seem to be favored in the P1' and P2' positions. The enzyme contains one atom of zinc and is inhibited by 1,10-phenanthroline, but not by EDTA. Iodoacetate, leupeptin, diisopropyl fluorophosphate, phenylmethylsulfonyl fluoride, pepstatin, and alpha 2-macroglobulin have no effect on enzyme activity. Disulfide reducing reagents, such as dithiothreitol or 2-mercaptoethanol, inactivate the enzyme completely. The partial amino-terminal sequence shows 46% identity with a **zinc metalloproteinase** from a strain of *Lysobacter enzymogenes* and 69% identity with the LasA protein from *Pseudomonas aeruginosa*.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: **Aeromonas hydrophila*--enzymology--EN; *Metalloendopeptidase s--isolation and purification--IP; Amino Acid Sequence; Chromatography, High Pressure Liquid; Electrophoresis, Polyacrylamide Gel; Hydrogen-Ion Concentration; Metalloendopeptidases--chemistry--CH; Metalloendopeptidases -- **genetics** --GE; Metalloendopeptidases--metabolism--ME; Molecular Sequence Data; Sequence Homology, Amino Acid; Substrate Specificity

Enzyme No.: EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.4 (microbial metalloproteinases)

Record Date Created: 19930514

8/9/7

DIALOG(R) File 155:MEDLINE(R)

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07456272 92390438 PMID: 1518864

Sequence analysis of rat mitochondrial intermediate peptidase : similarity to zinc metallopeptidases and to a putative yeast homologue.

Isaya G; Kalousek F; Rosenberg L E

Department of Genetics, Yale University School of Medicine, New Haven, CT 06510.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Sep 1 1992, 89 (17) p8317-21, ISSN 0027-8424
Journal Code: 7505876

Contract/Grant No.: DK09527; DK; NIDDK

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Proteolytic removal of amino-terminal octapeptides from mitochondrial intermediate proteins is a required step for a subgroup of nuclear-encoded mitochondrial precursors and is specifically catalyzed by mitochondrial intermediate peptidase (MIP). We recently reported the purification of MIP from rat liver and showed that the enzyme is a monomer of 75 kDa. We now report the sequence of a full-length rat MIP **cDNA**. This **cDNA** codes for a protein of 710 amino acids, including an amino-terminal mitochondrial leader peptide of 33 residues. The region surrounding the mature MIP amino terminus shows a cleavage site typically recognized by the **general** mitochondrial processing peptidase (MPP). In vitro synthesized MIP precursor is cleaved to mature MIP by purified MPP, and thus MIP is not required for its own proteolytic maturation. Comparison of the deduced MIP sequence with other sequences in the GenBank data base reveals two important similarities. The first is to a sequence encoding a putative MIP homologue in the recently reported sequence of yeast chromosome III. The putative yeast protein is predicted to be 712 amino acids long and includes a putative 23-residue mitochondrial leader peptide also with a MPP processing site. It shows 47% similarity and 24% identity to rat MIP. The second similarity is to members of a subfamily of metallopeptidases that includes rat metalloendopeptidase EC 3.4.24.15 and two bacterial proteases, oligopeptidase A and dipeptidyl carboxypeptidase. A region of greater than 50% similarity over 400 residues between MIP and these proteins is centered around the sequence motif HEXXH, typical of zinc metallopeptidases.

Tags: Animal; Comparative Study; Support, U.S. Gov't, P.H.S.

Descriptors: Endopeptidases-- **genetics** --GE; *Mitochondria, Liver --enzymology--EN; Amino Acid Sequence; Base Sequence; Blotting, Southern;

Cloning, Molecular; **DNA -- genetics** --GE; Endopeptidases--chemistry--CH;
Genes , Structural; Molecular Sequence Data; Protein Precursors
--metabolism--ME; Rats; Sequence Alignment
Molecular Sequence Databank No.: GENBANK/M61142; GENBANK/M84574;
GENBANK/M96633; GENBANK/X57947; GENBANK/X59720
CAS Registry No.: 0 (Protein Precursors); 9007-49-2 (DNA)
Enzyme No.: EC 3.4.- (Endopeptidases); EC 3.4.24.59 (mitochondrial
intermediate peptidase)
Record Date Created: 19921007

8/9/8

DIALOG(R) File 155:MEDLINE(R)

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06795757 91115060 PMID: 2276609

Cloning, nucleotide sequence and amplified expression of the gene encoding the extracellular metallo (Zn) DD- peptidase of Streptomyces albus G.

Duez C; Lakaye B; Houba S; Dusart J; Ghuysen J M

Service de Microbiologie, Universite de Liege, Sart Tilman, Belgium.

FEMS microbiology letters (NETHERLANDS) Sep 1 1990, 59 (1-2) p215-9,
ISSN 0378-1097 Journal Code: 7705721

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The **gene** encoding the extracellular metallo (Zn) DD- **peptidase** of *Streptomyces albus G* has been cloned in *Escherichia coli* DH5 alpha MCR via pBR322 or 325, and then transferred into *Streptomyces lividans* TK24 via pIJ486, with substantial amplification of the expressed DD-peptidase. The **gene** has the information for the synthesis of a 255 amino acid precursor, the amino terminal region of which has the characteristic features of a signal peptide. The primary structure as deduced from **nucleotide** sequencing confirms that previously determined by chemical methods except for the occurrence of an Asp instead of Asn at position 1 and an additional Ala immediately downstream of Pro67.

Tags: Support, Non-U.S. Gov't

Descriptors: Muramoylpentapeptide Carboxypeptidase-- **genetics** --GE;
Streptomyces*-- **genetics --GE; Amino Acid Sequence; Base Sequence; Cloning,
Molecular; Enzyme Precursors--biosynthesis--BI; Enzyme Precursors--
genetics --GE; *Escherichia coli*-- **genetics** --GE; Molecular Sequence Data;
Muramoylpentapeptide Carboxypeptidase--biosynthesis--BI; Muramoylpentapeptide Carboxypeptidase--metabolism--ME; Protein Sorting Signals-- **genetics** --GE; *Streptomyces*--enzymology--EN

CAS Registry No.: 0 (Enzyme Precursors); 0 (Protein Sorting Signals)

Enzyme No.: EC 3.4.17.8 (Muramoylpentapeptide Carboxypeptidase)

Record Date Created: 19910307

8/9/9

DIALOG(R) File 155:MEDLINE(R)

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06433607 90148980 PMID: 2302386

Primary structure of a zinc protease from Bacillus mesentericus strain 76.

Stoeva S; Kleinschmidt T; Mesrob B; Braunitzer G

Max-Planck-Institut fur Biochemie, Abteilung Proteinchemie, Martinsried bei Muenchen, West Germany.

Biochemistry (UNITED STATES) Jan 16 1990, 29 (2) p527-34, ISSN 0006-2960 Journal Code: 0370623

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The amino acid sequence of the neutral **zinc protease** from *Bacillus mesentericus* strain 76 (MCP 76) has been determined by using peptides derived from digests with trypsin, chymotrypsin, and cyanogen bromide and from cleavage with o-iodosobenzoic acid. The peptides were purified by means of gel filtration and reversed-phase high-performance liquid chromatography and analyzed by automatic sequencing. The protein contains 300 amino acid residues. It proved to be identical with the neutral protease deduced from the **DNA** precursor sequence of *Bacillus subtilis*. The residues for zinc and substrate binding are conserved, whereas the number of calcium binding sites is reduced compared to thermolysin. A classification of the neutral **zinc protease** is discussed.

Tags: Support, Non-U.S. Gov't

Descriptors: **Bacillus*--enzymology--EN; *Metalloendopeptidases; Amino Acid Sequence; Carboxypeptidases; Chromatography, Gel; Chromatography, High Pressure Liquid; Chymotrypsin; Iodobenzoates; Molecular Sequence Data; Peptide Fragments; Trypsin

CAS Registry No.: 0 (Iodobenzoates); 0 (Peptide Fragments); 304-91-6 (2-iodosobenzoic acid)

Enzyme No.: EC 3.4.- (Carboxypeptidases); EC 3.4.17.1 (carboxypeptidase A); EC 3.4.21.1 (Chymotrypsin); EC 3.4.21.4 (Trypsin); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.4 (microbial metalloproteinases)

Record Date Created: 19900326

8/9/10

DIALOG(R) File 155:MEDLINE(R)

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06088626 89174587 PMID: 2564389

Amino acid sequence deduced from a rat kidney cDNA suggests it encodes the Zn - peptidase aminopeptidase N.

Watt V M; Yip C C

Department of Physiology, University of Toronto, Canada.

Journal of biological chemistry (UNITED STATES) Apr 5 1989, 264 (10) p5480-7, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

We have isolated and characterized rat kidney **cDNA** clones encoding a 140-kDa glycoprotein that exhibits characteristics of a cell surface **Zn - peptidase**. Structural features predicted for this putative kidney **Zn - peptidase** (KZP) are most consistent with properties previously determined for the **Zn - peptidase** aminopeptidase N. The deduced amino acid sequence of rat KZP is almost identical to the NH2-terminal sequence of aminopeptidase N purified from rabbit. The overall amino acid composition predicted for rat KZP is remarkably similar to that previously determined for rabbit and pig aminopeptidase N. The predicted Mr of rat kidney KZP approximates the Mr of the unglycosylated form of aminopeptidase N. The topology predicted for KZP is identical to that observed for aminopeptidase N: a short cytoplasmic domain at the NH2 terminus immediately precedes an uncleaved signal/anchor domain; a stalk region connects this membrane anchor to the extracellular, hydrophilic bulk of the protein containing catalytic sites required for **Zn - peptidase** activity. In addition, mRNA encoding KZP is present in tissues known to exhibit aminopeptidase N activity. Taken together with the observation that only a single **gene** homologous to KZP **DNA** is present in the rat and human genomes, these results suggest that we have established the primary structure of rat kidney aminopeptidase N.

Tags: Animal; Comparative Study; Support, Non-U.S. Gov't

Descriptors: Aminopeptidases-- **genetics** --GE; * **DNA** -- **genetics** --GE; * **Genes**, Structural; *Kidney Cortex--enzymology--EN; Amino Acid Sequence; Aminopeptidases--isolation and purification--IP; Antigens, CD13; Base Sequence; Cell Membrane--enzymology--EN; Cloning, Molecular; **DNA**

--isolation and purification--IP; Molecular Sequence Data; Molecular Weight
; Rats; Sequence Homology, **Nucleic Acid**
Molecular Sequence Databank No.: GENBANK/M25073
CAS Registry No.: 9007-49-2 (DNA)
Enzyme No.: EC 3.4.11 (Aminopeptidases); EC 3.4.11.2 (Antigens, CD13)
Record Date Created: 19890511

8/9/11

DIALOG(R) File 155:MEDLINE(R)

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05025537 86103356 PMID: 3910041

Protease **susceptibility of zinc - and apo-carboxypeptidase A.**

Bicknell R; Schaeffer A; Auld D S; Riordan J F; Monnanni R; Bertini I
Biochemical and biophysical research communications (UNITED STATES) Dec
17 1985, 133 (2) p787-93, ISSN 0006-291X Journal Code: 0372516

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Proteases in preparations of carboxypeptidase A progressively inactivate solutions of the apoenzyme but not the metal-containing enzyme. Free amino acids **generated** by proteolysis interfere with spectral studies after reconstituting the apoenzyme with cobalt. Purification by affinity chromatography eliminates this effect. Affinity-purified apoenzyme is susceptible to digestion with chymotrypsin but the metalloenzyme is not.

Descriptors: *Apoenzymes--metabolism--ME; *Apoproteins--metabolism--ME; *Carboxypeptidases--metabolism--ME; *Peptide Hydrolases--metabolism--ME; Chemistry; Chromatography, Affinity; Crystallization; Solutions; Spectrophotometry; Zinc

CAS Registry No.: 0 (Apoenzymes); 0 (Apoproteins); 0 (Solutions); 7440-66-6 (Zinc)

Enzyme No.: EC 3.4 (Peptide Hydrolases); EC 3.4.- (Carboxypeptidases); EC 3.4.17.1 (carboxypeptidase A)

Record Date Created: 19860127

8/9/12

DIALOG(R) File 155:MEDLINE(R)

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04005756 83000262 PMID: 7052122

Structure of a mercaptan-thermolysin complex illustrates mode of inhibition of zinc proteases by substrate-analogue mercaptans.

Monzingo A F; Matthews B W

Biochemistry (UNITED STATES) Jul 6 1982, 21 (14) p3390-4, ISSN 0006-2960 Journal Code: 0370623

Contract/Grant No.: GM 20066; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The structure of the complex of thermolysin and the inhibitor (2-benzyl-3-mercaptopropanoyl)-L-alanylglycinamide has been determined by X-ray crystallography at a resolution of 1.9 Å and refined to a crystallographic residual of 18.4%. The binding of this potent, specific inhibitor to thermolysin ($K_i = 7.5 \times 10^{-7}$ M) serves as a model for the inhibition of **zinc peptidases** by substrate-analogue mercaptans. The study shows that the mercaptan inhibitor binds to thermolysin with the sulfur, presumably in the anionic form, tetrahedrally coordinated to the zinc and displacing a water molecule bound to the native enzyme. This is the first direct determination of the mode of binding of a mercaptan inhibitor to a **zinc peptidase** and confirms the geometry of binding expected on **general** grounds [Ondetti, M. A., Condon, M. E., Reid, J.,

Sabo, E. F., Cheung, H. S., & Cushman, D. W. (1979) Biochemistry 18, 1427-1430; Nishino, N., & Powers, J. C. (1979) Biochemistry 18, 4340-4347] and inferred from previous spectroscopic studies [Holmquist, B., & Vallee, B. L. (1979) Proc. Natl. Acad. Sci. U.S.A. 76, 6216-6220].

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *Protease Inhibitors; *Protease Inhibitors--metabolism--ME; *Sulfhydryl Compounds--metabolism--ME; *Thermolysin--metabolism--ME; 3-Mercaptopropionic Acid--analogs and derivatives--AA; 3-Mercaptopropionic Acid--pharmacology--PD; Binding Sites; Kinetics; Metalloendopeptidases; Models, Molecular; Zinc--metabolism--ME

CAS Registry No.: 0 (Protease Inhibitors); 0 (Sulfhydryl Compounds); 107-96-0 (3-Mercaptopropionic Acid); 71431-51-1 (2-benzyl-3-mercaptopropionyl-alanylglycinamide); 7440-66-6 (Zinc)

Enzyme No.: EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.27 (Thermolysin)

Record Date Created: 19821202

?logoff hold

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\$2.52 12 Type(s) in Format 9

\$2.52 12 Types

\$7.93 Estimated cost File155

\$0.92 TELNET

\$8.85 Estimated cost this search

\$8.85 Estimated total session cost 1.850 DialUnits

Status: Signed Off. (4 minutes)

09124949 97014153 PMID: 8860988

The metzincin-superfamily of zinc - peptidases .

* Bode W; Grams F; Reinemer P; Gomis-Ruth F X; Baumann U; McKay D B;
* Stocker W

~ Max-Planck-Institut fur Biochemie, Am Klopferspitz, Martinsried, Germany.

* Advances in experimental medicine and biology (UNITED STATES) 1996,
389 p1-11, ISSN 0065-2598 Journal Code: 0121103

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

(49 Refs.)

Tags: Support, Non-U.S. Gov't

Descriptors: Metalloendopeptidases-- **genetics** --GE; *Multigene Family;
Amino Acid Sequence; Binding Sites; Catalysis; Metalloendopeptidases
--chemistry--CH; Models, Molecular; Molecular Sequence Data; Sequence
Homology, Amino Acid; Structure-Activity Relationship

Enzyme No.: EC 3.4.24 (Metalloendopeptidases)

Record Date Created: 19970306